From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44*bis*.3(c) and 72.2)

To:

RUFF, WILHELM, BEIER, DAUSTER & PARTNER
Kronenstrasse 30
70174 Stuttgart
ALLEMAGNE

Verfrist:
Hauptfrist:
Erledigt:

Date of mailing (*day/month/year*)
12 October 2006 (12.10.2006)

Eingegangen
18. Okt. 2006
Patentanwälte

Applicant's or agent's file reference
P 43831 WO

IMPORTANT NOTIFICATION

International application No.
PCT/EP2005/001567

International filing date (*day/month/year*)
16 February 2005 (16.02.2005)

Applicant
PROTEOSYS AG et al

1. **Transmittal of the translation to the applicant.**

☑ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).

☐ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. **Transmittal of the copy of the translation to the designated or elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference P 43831 WO	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/EP2005/001567	International filing date *(day/month/year)* 16 February 2005 (16.02.2005)	Priority date *(day/month/year)* 16 February 2004 (16.02.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant PROTEOSYS AG		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 16 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 04 October 2006 (04.10.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Yolaine Cussac e-mail: pt11@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	See form PCT/ISA/210
Applicant's or agent's file reference: P 43831 WO	FOR FURTHER ACTION: See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2005/001567	16.02.2005	16.02.2004

International Patent Classification (IPC) or both national classification and IPC
A61P35/00, G01N33/574

Applicant
PROTEOSYS AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☒ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/EP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/001567

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 15-26 (in full) and 5,6,9,10,13,14,27-53 (in part)

because:

☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 5,6,9,10,36-47,49-52 (in part) are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 15-26 (in full) and 13,14,27-37,46-53 (in part)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☒ See Supplemental Box for further details.

WRITTEN OPINION OF THE
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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:

   ☒ paid additional fees

   ☐ paid additional fees under protest

   ☐ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   See supplemental sheet

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☐ all parts

   ☒ the parts relating to claims Nos. 1-12, 38, 39 (in full) and 13, 14, 27-37, 46-51, 53 (in part)

WRITTEN OPINION OF THE
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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims		YES
	Claims	1-12, 38, 39 (all) and 13, 14, 27-37, 46-51, 53 (in part)	NO
Inventive step (IS)	Claims		YES
	Claims	1-12, 38, 39 (all) and 13, 14, 27-37, 46-51, 53 (in part)	NO
Industrial applicability (IA)	Claims	1-12, 38, 39 (all) and 13, 14, 27-37, 46-51, 53 (in part)	YES
	Claims		NO

2. Citations and explanations:

Reference is made to the following documents:

D1 US 2002/119463 A1 (FARIS MARY ET AL) 29 August 2002

D2 US-B1-6 476 207 (ZHANG JIMMY ET AL) 5 November 2002

D3 US 2003/108963 A1 (SCHLEGEL ROBERT ET AL) 12 June 2003

D4 HOFMANN E A: "Interactions of benzodiazepine derivatives with annexins" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 273, 5, 30 January 1998 (1998-01-30), pages 2885-2894, XP002098631 ISSN: 0021-9258

D5 US 2003/185808 A1 (THRAVES PETER ET AL) 2 October 2003 (2003-10-02)

D6 US 2003/180738 A1 (REES ROBERT CHARLES ET AL) 25 September 2003 (2003-09-25)

1 INVENTION 1

The present application does not meet the requirements of PCT Article 33(1) because the subject matter of claims 1-10, 31-36, 50, 51 and 53 is not novel under PCT Article 33(2) and/or not inventive under PCT Article

33(3).

1.1 INDEPENDENT CLAIMS 1, 5 and 53

Document D3 discloses (the references between parentheses relate to this document):

Use of the protein annexin A3 as a diagnostic marker for prostate cancer (pages 1-2 paragraphs 11, 15-18 and 22; pages 5-16 tables 1-4), as a target for the treatment of prostate cancer (pages 1-2 paragraphs 11, 15-18 and 22; pages 5-16 tables 1-4) and for the search for/ identification of active substances for the treatment of cancer (pages 35-37 paragraphs 221-231).

The subject matter of claims 1, 5 and 53 is therefore not novel.

1.2 INDEPENDENT CLAIM 36

Document D3 discloses (the references between parentheses relate to this document):

Diagnosis kit (page 4 paragraphs 58, 59 and 61), comprising at least one substance for detecting the activity and/or abundance of annexin A3 for the recognition of prostate cancer (pages 3-4 paragraphs 57-59 and 61).

The subject matter of claim 36 is therefore not novel.

1.3 DEPENDENT CLAIMS 2-4, 6-8, 31-35, 50 and 51

Claims 2-4, 6-8, 31-35, 50 and 51 do not contain any features which, in combination with the features of any claim to which they refer back, meet the PCT

requirements for novelty and inventive step.

2 INVENTION 2

The present application does not meet the requirements of PCT Article 33(1) because the subject matter of claims 11, 12, 28-30, 36, 38, 39, 46-49, 51 and 53 is not inventive under PCT Article 33(3).

2.1 INDEPENDENT CLAIMS 11, 28, 38 and 53

2.1.1 Document D3 is considered to be the closest prior art with respect to the subject matter of claims 11, 28, 36, 38 and 53. It discloses (the references between parentheses relate to this document):

Use of the protein annexin A3 as a diagnostic marker for prostate cancer (pages 1-2 paragraphs 11, 15-18 and 22; pages 5-16 tables 1-4), as a target for the treatment of prostate cancer (pages 1-2 paragraphs 11, 15-18 and 22; pages 5-16 tables 1-4), and for the search for/ identification of active substances for the treatment of cancer (pages 35-37 paragraphs 221-231).

2.1.2 The subject matter of claims 11, 28, 36, 38 and 53 of invention 2 differs from D3 by the use of enoyl coenzyme A hydratase as a target for the treatment of prostate cancer. No technical effect is evident from this difference.

2.1.3 The problem addressed by the present invention can therefore be considered as: how can a further process for the treatment/diagnosis and for the search for/identification of active substances for the treatment of prostate cancer be provided?

2.1.4 The solution proposed in claims 11, 28, 38 and 53 cannot be considered to be inventive. The reason for this is that differential expression of enoyl coenzyme A hydratase in prostate cancer cell cultures is already known from D5 (see D5 paragraphs 1, 2, 5, 8-15, 34, and also table 1 in paragraph 86 on page 6). A person practised in the art would therefore combine the teaching present in D3 and D5 without thereby being inventive in order to arrive at the solution proposed in invention 2.

2.2 INDEPENDENT CLAIM 36

The lack of inventive step detailed above for claims 11, 28, 38 and 53 also applies *mutatis mutandis* to claim 36, which is therefore not considered to be inventive either.

2.3 DEPENDENT CLAIMS 12, 29, 30, 39, 46-49 and 51

Claims 12, 29, 30, 39, 46-49 and 51 do not contain any features which, in combination with the features of any claim to which they refer back, meet the PCT requirements for novelty and inventive step.

3 INVENTION 4

The present application does not meet the requirements of PCT Article 33(1) because the subject matter of claims 13, 14, 27-30, 36, 37, 46-51 and 53 is not novel under PCT Article 33(2) and/or not inventive under PCT Article 33(3).

3.1 INDEPENDENT CLAIMS 13, 27, 28, 37 and 53

Document D6 discloses (the references between parentheses relate to this document):

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Use of ubiquitin isopeptidase T as a diagnostic marker for prostate cancer (paragraphs 1, 7 and 21 and claims 1-21, together with SEQ ID 54 on page 12), as a target for the treatment of prostate cancer (paragraphs 1, 7 and 26 and claims 1-21 together with SEQ ID 54 on page 12), and for the search for/identification of active substances for the treatment of prostate cancer (paragraphs 1, 7 and 36 and claims 1-21 together with SEQ ID 54 on page 12).

The subject matter of claims 13, 27, 28, 37 and 53 is therefore not novel.

3.2 INDEPENDENT CLAIM 36

Document D6 discloses (the references between parentheses relate to this document):

Diagnosis kit (paragraphs 1, 7 and 25 together with SEQ ID 54 on page 12), comprising at least one substance for detecting the activity and/or abundance of ubiquitin isopeptidase T for the recognition of prostate cancer (paragraphs 1, 7 and 25 together with SEQ ID 54 on page 12).

The subject matter of claim 36 is therefore not novel.

3.3 DEPENDENT CLAIMS 14, 29, 30 and 46-51

Claims 14, 29, 30 and 46-51 do not contain any features which, in combination with the features of any claim to which they refer back, meet the PCT requirements for novelty and inventive step.

4 INDUSTRIAL APPLICABILITY

The present application meets the requirements of PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/001567

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Article 33(1) because the subject matter of the claims of inventions 1, 2 and 4 is industrially applicable under PCT Article 33(4).

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

Box III

The current claims 5, 6, 9, 10, 36-47 and 49-52 relate to an inordinately large number of possible compounds, of which only a small proportion are supported by the description (PCT Article 6) and/or can be regarded as having been disclosed in the application (PCT Article 5). The search and the examination were therefore directed to the parts of the claims that appear to be supported and disclosed in the above sense, namely the parts relating to: benzodiazepine derivatives (page 36 lines 1-14), annexin A3-specific antibodies (page 36 lines 16-23), antisense molecules (page 42 line 17) and therapeutic antibodies (page 42 line 28).

Box IV

The different inventions/groups of inventions are:

1 1-10 (all) and 31-36, 50, 51, 53 (in part)
Use of annexin A3 as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

2 11, 12, 38, 39 (all) and 28-30, 36, 46-49, 51, 53 (in part)
Use of enoyl coenzyme A hydratase as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

3 13-14, 28-30, 37, 46-49, 51 (all in part)
Use of protein disulfide isomerase (PDI) as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

Supplemental Box

4 13, 14, 27-30, 36, 37, 46-51, 53 (all in part)
Use of ubiquitin isopeptidase T as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

5 15, 16, 40 (all) and 27, 31-36, 41, 46-49, 51, 53 (in part)
Use of serum amyloid P component (SAP) as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

6 17, 18, 41 (all) and 31-36, 41, 46-49, 51, 53 (in part)
Use of nuclear chloride ion channel protein as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

7 19, 20, 42 (all) and 46-49, 51, 53 (in part)
Use of HES1 as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

8 21, 22, 43 (all) and 46-49, 51, 53 (in part)
Use of proteasome alpha 2 subunit as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

9 23, 24, 44 (all) and 46-49, 51, 53 (in part)
Use of adenine phosphoribosyl transferase as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

10 25, 26, 45 (all) and 46-49, 51, 53 (in part)
Use of inorganic pyrophosphatase as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

Supplemental Box

11 28-30, 50, 51 (all in part)
Use of heat shock protein 27 (HSP27) as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

12 28-30, 50, 51 (all in part)
Use of heat shock protein 90 (HSP90) as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

13 28-30, 51 (all in part)
Use of nucleophosmin as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

14 31-35, 50, 51 (all in part)
Use of fatty acid-binding protein 3 (FAB 3) as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

15 31-35, 50, 51 (all in part)
Use of galectin as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

16 31-35, 50, 51 (all in part)
Use of microseminoprotein beta as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

17 31-35, 51 (all in part)
Use of 14-3-3 portein beta as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

Supplemental Box

18 31-35, 51 (all in part)
Use of 14-3-3 protein zeta as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

19 31-35, 51, 53 (all in part)
Use of 14-3-3 protein tau as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

20 31, 33-35, 51 (all in part)
Use of epidermal fatty acid-binding protein (E-FABP) as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

21 31-35, 50, 51 (all in part)
Use of transgelin as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

22 31-35, 51 (all in part)
Use of triose phosphate isomerase as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

23 31-35, 51 (all in part)
Use of aldolase A as a diagnostic marker for prostate cancer and as a target for the treatment of prostate cancer.

These inventions/groups are not so linked as to form a single general inventive concept for the following reasons (PCT Rule 13.1):

Supplemental Box

The technical problem to be solved by the present application is concerned with the provision of methods for the diagnosis and treatment of prostate cancer. The only general concept which is shared by each invention claimed and which can be considered to be a solution for the above problem can be defined *a priori* as "use of certain genes/proteins as a marker for the diagnosis and treatment of prostate cancer".

Such methods are, however, already known:

D1 describes the use of genes/gene products which are expressed differentially in prostate cancer tissue as a marker for the diagnosis and treatment of patients with prostate cancer (see D1, paragraphs 1 and 10-14).

D2 likewise describes the use of genes/gene products which are expressed differentially in prostate cancer tissue as marker for the diagnosis and treatment of patients with prostate cancer (see D2, column 1 line 10 - column 2 line 55).

Taking account of the discoveries in D1 or D2, the above-identified single general concept cannot be considered to be novel and inventive and therefore does not meet the prerequisites to be "the single general inventive concept" as required by PCT Rule 13.1. The present application therefore does not meet the prerequisites for unity of the invention, as described in PCT Rule 13.1.

It was not possible to identify any other technical feature which can establish a technical connection between the different inventions claimed and which can be considered as a result as a "special technical feature" under PCT Rule 13.2.

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum
Internationales Büro

PCT

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16. Februar 2005 (16.02.2005)

(25) Einreichungssprache: Deutsch

(26) Veröffentlichungssprache: Deutsch

(30) Angaben zur Priorität:
10 2004 008 449.1
16. Februar 2004 (16.02.2004) DE
10 2004 038 076.7 29. Juli 2004 (29.07.2004) DE

(71) Anmelder *(für alle Bestimmungsstaaten mit Ausnahme von US)*: **PROTEOSYS AG** [DE/DE]; Carl-Zeiss-Strasse 51, 55129 Mainz (DE).

(72) Erfinder; und

(75) Erfinder/Anmelder *(nur für US)*: **CAHILL, Michael** [DE/DE]; Weinbergstrasse 34, 55296 Lützweiler (DE). **KLOCKER, Helmut** [AT/AT]; Ziegelstrasse 46a, A-6401 Inzing (AT). **ROGATSCH, Hermann** [AT/AT]; Hans-Untermüller-Strasse 5/12, A-6020 Innsbruck (AT).

(74) Anwalt: **RUFF, WILHELM, BEIER, DAUSTER & PARTNER**; Kronenstrasse 30, 70174 Stuttgart (DE).

(81) Bestimmungsstaaten *(soweit nicht anders angegeben, für jede verfügbare nationale Schutzrechtsart)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Bestimmungsstaaten *(soweit nicht anders angegeben, für jede verfügbare regionale Schutzrechtsart)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,

[Fortsetzung auf der nächsten Seite]

(54) Title: DIAGNOSTIC MARKER FOR CANCER

(54) Bezeichnung: DIAGNOSTISCHE MARKER FÜR KREBS

AA	BB Identifikation			CC 31 Patienten		CC 22/31 Patienten		CC 9/31 Patienten	
Nr.	Protein Name	Accession Nr.	PMF score	P-Wert DD	0 50 100	P-Wert DD	0 50 100	P-Wert DD	0 50 100
1	IsoT	gi|1732411	115	<0.0001		0.0006		0.0300	
2	SAP	gi|576259	106*	0.0001		0.0005		0.1398	
3	M-FABP	gi|494781	87	0.0048		0.0069		0.4640	
4	Galectin-1	gi|4504981	177*	0.0124		0.0105		0.4400	
5	HSP 27	gi|662641	162*	0.0007		0.0071		0.0050	
6	microseminoprotein	gi|225159	92*	0.0002		0.0002		0.1602	
7	Rho GDI	gi|4757768	150	0.0011		0.0005		0.9058	
8	14-3-3 zeta	gi|4507953	160*	0.0009		0.0003		0.6951	
9	14-3-3 beta	gi|4507949	160*	0.0016		0.0008		0.8253	
10	HSP 90, alpha	gi|13129150	147	0.0006		0.0005		0.4506	
	HSP 90, beta	gi|20149594	164						
11	14-3-3 tau	gi|5803227	130*	0.0028		0.0028		0.2661	
12	BIP/HspA5	gi|87528	273	0.1551		0.0075		0.1843	
13	PDI	gi|20070125	235	<0.0001		<0.0001		0.4575	
14	Annexin A3	gi|4826643	160	0.0453		0.0008		0.5030	
15	E-FABP	gi|4557581	94*	0.0009		0.0010		0.4807	
16	Enoyl-co A hydratase	gi|12707570	101*	<0.0001		<0.0001		0.2054	
17	Nucleophosmin	gi|16307090	77	0.0015		0.0001		0.8401	

AA No.
BB IDENTIFICATION
CC PATIENTS
DD P-VALUE

(57) Abstract: The invention relates to the use of various proteins as diagnostic markers for cancerous diseases. In particular, the use of the annexin A3 protein is preferred. Preferably an increased regulation of annexin A3 is analysed in comparison to controls. The invention also relates to the use of active substances for producing a medicament used in the treatment of cancer, said substances influencing the activity and/or abundance of various characteristic proteins.

(57) Zusammenfassung: Es wird die Verwendung verschiedener Proteine als diagnostische Marker für Krebserkrankungen bereitgestellt. Besonders bevorzugt ist die Verwendung des Proteins Annexin A3. Bevorzugterweise wird hierbei eine Heraufregulation von Annexin A3 im Vergleich mit Kontrollen untersucht. Weiterhin wird die Verwendung von Wirkstoffen zur Herstellung eines Medikaments zur Behandlung von Krebs beschrieben, wobei diese Wirkstoffe die Aktivität und/oder die Abundanz verschiedener charakteristischer Proteine beeinflussen.

WO 2005/078124 A3

ZM, ZW), eurasisches (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), europäisches (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Veröffentlicht:

— *mit internationalem Recherchenbericht*

(88) Veröffentlichungsdatum des internationalen Recherchenberichts: 10. August 2006

Zur Erklärung der Zweibuchstaben-Codes und der anderen Abkürzungen wird auf die Erklärungen ("Guidance Notes on Codes and Abbreviations") am Anfang jeder regulären Ausgabe der PCT-Gazette verwiesen.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/001567

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61P35/00 G01N33/574

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 476 207 B1 (ZHANG JIMMY ET AL) 5 November 2002 (2002-11-05) the whole document	1-53
A	US 2002/119463 A1 (FARIS MARY ET AL) 29 August 2002 (2002-08-29) the whole document	1-53
X	US 2003/108963 A1 (SCHLEGEL ROBERT ET AL) 12 June 2003 (2003-06-12)	1-7,9, 10, 31-36, 50,51,53
Y	the whole document	8
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 August 2005	15 SEP 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Angioni, C

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/001567

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HOFMANN E A: "Interactions of benzodiazepine drivatives with annexins" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 273, no. 5, 30 January 1998 (1998-01-30), pages 2885-2894, XP002098631 ISSN: 0021-9258 cited in the application the whole document	8
A	VAARALA M H ET AL: "Differentially expressed genes in two LNCaP prostate cancer cell lines REFLECTING CHANGES DURING PROSTATE CANCER PROGRESSION" LABORATORY INVESTIGATION, UNITED STATES AND CANADIAN ACADEMY OF PATHOLOGY, BALTIMORE,, US, vol. 80, no. 8, August 2000 (2000-08), pages 1259-1268, XP002225395 ISSN: 0023-6837 the whole document	1-53
X	US 2003/185808 A1 (THRAVES PETER ET AL) 2 October 2003 (2003-10-02) the whole document	11,12, 28-30, 36,38, 39, 46-49, 51,53
X	US 2003/180738 A1 (REES ROBERT CHARLES ET AL) 25 September 2003 (2003-09-25) the whole document	13,27, 29,30, 36,37, 46-51,53
P,X	GRANER EDGARD ET AL: "The isopeptidase USP2a regulates the stability of fatty acid synthase in prostate cancer" CANCER CELL, vol. 5, no. 3, March 2004 (2004-03), pages 253-261, XP002340626 ISSN: 1535-6108 the whole document	13,14, 27-30, 36,37, 46-51,53

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2005/001567

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See supplemental sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

1-12, 38, 39 (full) and 13, 14, 27-37, 46-51, 53 (in part)

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

The International Searching Authority has found that the international application contains multiple (groups of) inventions, as follows:

1. Claims: 1-10 (full) and 31-36, 50, 51, 53 (in part)

   Use of annexin A3 as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

   ---

2. Claims: 11, 12, 38, 39 (full) and 28-30, 36, 46-49, 51, 53 (in part)

   Use of enoyl coenzyme A hydratase as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

   ---

3. Claims: 13-14, 28-30, 37, 46-49, 51 (all in part)

   Use of protein disulfide isomerase (PDI) as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

   ---

4. Claims: 13, 14, 27-30, 36, 37, 46-51, 53 (all in part)

   Use of ubiquitin isopeptidase T as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

   ---

5. Claims: 15, 16, 40 (full) and 27, 31-36, 41, 46-49, 51, 53 (in part)

   Use of serum amyloid P component (SAP) as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

   ---

6. Claims: 17, 18, 41 (full) and 31-36, 41, 46-49, 51, 53 (in part)

   Use of nuclear chloride ion channel protein as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

   ---

7. Claims: 19, 20, 42 (full) and 46-49, 51, 53 (in part)

   Use of HBS1 as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

   ---

8. Claims: 21, 22, 43 (full) and 46-49, 51, 53 (in part)

Use of proteasome alpha-2 subunit as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

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9. Claims: 23, 24, 44 (full) and 46-49, 51, 53 (in part)

Use of adenine phosphoribosyl transferase as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

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10. Claims: 25, 26, 45 (full) and 46-49, 51, 53 (in part)

Use of inorganic pyrophosphatase as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

---

11. Claims: 28-30, 50, 51 (all in part)

Use of heat shock protein 27 (HSP27) as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

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12. Claims: 28-30, 50, 51 (all in part)

Use of heat shock protein 90 (HSP90) as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

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13. Claims: 28-30, 51 (all in part)

Use of nucleophosmin as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

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14. Claims: 31-35, 50, 51 (all in part)

Use of fatty acid binding protein 3 (FABP-3) as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

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15. Claims: 31-35, 50, 51 (all in part)

Use of galectin as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

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16. Claims: 31-35, 50, 51 (all in part)

Use of microseminoprotein beta as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

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17. Claims: 31-35, 51 (all in part)

Use of 14-3-3 protein beta as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

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18. Claims: 31-35, 51 (all in part)

Use of 14-3-3 protein zeta as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

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19. Claims: 31-35, 51, 53 (all in part)

Use of 14-3-3 protein tau as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

---

20. Claims: 31, 33-35, 51 (all in part)

Use of epidermal fatty acid-binding protein (E-FABP) as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

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21. Claims: 31-35, 50, 51 (all in part)

Use of transgelin as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

---

22. Claims: 31-35, 51 (all in part)

Use of triosephosphate isomerase as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

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23. Claims: 31-35, 51 (all in part)

Use of aldolase A as diagnostic marker for prostate cancer and as target for the treatment of prostate cancer.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP2005/001567

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6476207 B1	05-11-2002	EP 1466988 A2	13-10-2004
		EP 1086218 A2	28-03-2001
		JP 2002517244 T	18-06-2002
		WO 9964594 A2	16-12-1999
		US 2002192699 A1	19-12-2002
		AU 4435899 A	30-12-1999
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US 2003108963 A1	12-06-2003	US 2005191673 A1	01-09-2005
		WO 03009814 A2	06-02-2003
US 2003185808 A1	02-10-2003	AT 259655 T	15-03-2004
		AU 4434101 A	15-10-2001
		AU 4935600 A	12-12-2000
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		CA 2374294 A1	30-11-2000
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		DE 60008368 D1	25-03-2004
		DE 60008368 T2	09-12-2004
		EP 1178822 A2	13-02-2002
		EP 1272617 A2	08-01-2003
		ES 2215662 T3	16-10-2004
		WO 0071155 A2	30-11-2000
		WO 0071156 A2	30-11-2000
		WO 0175073 A2	11-10-2001
		JP 2003500366 T	07-01-2003
US 2003180738 A1	25-09-2003	AU 2692201 A	31-07-2001
		CA 2397910 A1	26-07-2001
		EP 1250457 A2	23-10-2002
		WO 0153524 A2	26-07-2001

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2005/001567

A. KLASSIFIZIERUNG DES ANMELDUNGSGEGENSTANDES
IPK 7 A61P35/00 G01N33/574

Nach der Internationalen Patentklassifikation (IPK) oder nach der nationalen Klassifikation und der IPK

B. RECHERCHIERTE GEBIETE

Recherchierter Mindestprüfstoff (Klassifikationssystem und Klassifikationssymbole)
IPK 7 G01N

Recherchierte aber nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Gebiete fallen

Während der Internationalen Recherche konsultierte elektronische Datenbank (Name der Datenbank und evtl. verwendete Suchbegriffe)
EPO-Internal, BIOSIS, EMBASE

C. ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
A	US 6 476 207 B1 (ZHANG JIMMY ET AL) 5. November 2002 (2002-11-05) das ganze Dokument	1-53
A	US 2002/119463 A1 (FARIS MARY ET AL) 29. August 2002 (2002-08-29) das ganze Dokument	1-53
X	US 2003/108963 A1 (SCHLEGEL ROBERT ET AL) 12. Juni 2003 (2003-06-12)	1-7,9, 10, 31-36, 50,51,53
Y	das ganze Dokument	8

-/—

[X] Weitere Veröffentlichungen sind der Fortsetzung von Feld C zu entnehmen

[X] Siehe Anhang Patentfamilie

* Besondere Kategorien von angegebenen Veröffentlichungen :
"A" Veröffentlichung, die den allgemeinen Stand der Technik definiert, aber nicht als besonders bedeutsam anzusehen ist
"E" älteres Dokument, das jedoch erst am oder nach dem internationalen Anmeldedatum veröffentlicht worden ist
"L" Veröffentlichung, die geeignet ist, einen Prioritätsanspruch zweifelhaft erscheinen zu lassen, oder durch die das Veröffentlichungsdatum einer anderen im Recherchenbericht genannten Veröffentlichung belegt werden soll oder die aus einem anderen besonderen Grund angegeben ist (wie ausgeführt)
"O" Veröffentlichung, die sich auf eine mündliche Offenbarung, eine Benutzung, eine Ausstellung oder andere Maßnahmen bezieht
"P" Veröffentlichung, die vor dem internationalen Anmeldedatum, aber nach dem beanspruchten Prioritätsdatum veröffentlicht worden ist
"T" Spätere Veröffentlichung, die nach dem internationalen Anmeldedatum oder dem Prioritätsdatum veröffentlicht worden ist und mit der Anmeldung nicht kollidiert, sondern nur zum Verständnis des der Erfindung zugrundeliegenden Prinzips oder der ihr zugrundeliegenden Theorie angegeben ist
"X" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann allein aufgrund dieser Veröffentlichung nicht als neu oder auf erfinderischer Tätigkeit beruhend betrachtet werden
"Y" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann nicht als auf erfinderischer Tätigkeit beruhend betrachtet werden, wenn die Veröffentlichung mit einer oder mehreren anderen Veröffentlichungen dieser Kategorie in Verbindung gebracht wird und diese Verbindung für einen Fachmann naheliegend ist
"&" Veröffentlichung, die Mitglied derselben Patentfamilie ist

Datum des Abschlusses der internationalen Recherche	Absendedatum des internationalen Recherchenberichts
15. August 2005	15 SEP 2005

Name und Postanschrift der Internationalen Recherchenbehörde	Bevollmächtigter Bediensteter
Europäisches Patentamt, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Angioni, C

Formblatt PCT/ISA/210 (Blatt 2) (Januar 2004)

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2005/001567

C.(Fortsetzung) ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
Y	HOFMANN E A: "Interactions of benzodiazepine drivatives with annexins" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, Bd. 273, Nr. 5, 30. Januar 1998 (1998-01-30), Seiten 2885-2894, XP002098631 ISSN: 0021-9258 in der Anmeldung erwähnt das ganze Dokument	8
A	VAARALA M H ET AL: "Differentially expressed genes in two LNCaP prostate cancer cell lines REFLECTING CHANGES DURING PROSTATE CANCER PROGRESSION" LABORATORY INVESTIGATION, UNITED STATES AND CANADIAN ACADEMY OF PATHOLOGY, BALTIMORE,, US, Bd. 80, Nr. 8, August 2000 (2000-08), Seiten 1259-1268, XP002225395 ISSN: 0023-6837 das ganze Dokument	1-53
X	US 2003/185808 A1 (THRAVES PETER ET AL) 2. Oktober 2003 (2003-10-02) das ganze Dokument	11,12, 28-30, 36,38, 39, 46-49, 51,53
X	US 2003/180738 A1 (REES ROBERT CHARLES ET AL) 25. September 2003 (2003-09-25) das ganze Dokument	13,27, 29,30, 36,37, 46-51,53
P,X	GRANER EDGARD ET AL: "The isopeptidase USP2a regulates the stability of fatty acid synthase in prostate cancer" CANCER CELL, Bd. 5, Nr. 3, März 2004 (2004-03), Seiten 253-261, XP002340626 ISSN: 1535-6108 das ganze Dokument	13,14, 27-30, 36,37, 46-51,53

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2005/001567

Feld II Bemerkungen zu den Ansprüchen, die sich als nicht recherchierbar erwiesen haben (Fortsetzung von Punkt 2 auf Blatt 1)

Gemäß Artikel 17(2)a) wurde aus folgenden Gründen für bestimmte Ansprüche kein Recherchenbericht erstellt:

1. ☐ Ansprüche Nr.
weil sie sich auf Gegenstände beziehen, zu deren Recherche die Behörde nicht verpflichtet ist, nämlich

2. ☐ Ansprüche Nr.
weil sie sich auf Teile der internationalen Anmeldung beziehen, die den vorgeschriebenen Anforderungen so wenig entsprechen, daß eine sinnvolle internationale Recherche nicht durchgeführt werden kann, nämlich

3. ☐ Ansprüche Nr.
weil es sich dabei um abhängige Ansprüche handelt, die nicht entsprechend Satz 2 und 3 der Regel 6.4 a) abgefaßt sind.

Feld III Bemerkungen bei mangelnder Einheitlichkeit der Erfindung (Fortsetzung von Punkt 3 auf Blatt 1)

Die Internationale Recherchenbehörde hat festgestellt, daß diese internationale Anmeldung mehrere Erfindungen enthält:

siehe Zusatzblatt

1. ☐ Da der Anmelder alle erforderlichen zusätzlichen Recherchengebühren rechtzeitig entrichtet hat, erstreckt sich dieser Internationale Recherchenbericht auf alle recherchierbaren Ansprüche.

2. ☐ Da für alle recherchierbaren Ansprüche die Recherche ohne einen Arbeitsaufwand durchgeführt werden konnte, der eine zusätzliche Recherchengebühr gerechtfertigt hätte, hat die Behörde nicht zur Zahlung einer solchen Gebühr aufgefordert.

3. ☒ Da der Anmelder nur einige der erforderlichen zusätzlichen Recherchengebühren rechtzeitig entrichtet hat, erstreckt sich dieser Internationale Recherchenbericht nur auf die Ansprüche, für die Gebühren entrichtet worden sind, nämlich auf die Ansprüche Nr.
1-12, 38, 39 (ganz) und 13, 14, 27-37, 46-51, 53 (zum Teil)

4. ☐ Der Anmelder hat die erforderlichen zusätzlichen Recherchengebühren nicht rechtzeitig entrichtet. Der Internationale Recherchenbericht beschränkt sich daher auf die in den Ansprüchen zuerst erwähnte Erfindung; diese ist in folgenden Ansprüchen erfaßt:

Bemerkungen hinsichtlich eines Widerspruchs

☐ Die zusätzlichen Gebühren wurden vom Anmelder unter Widerspruch gezahlt.

☒ Die Zahlung zusätzlicher Recherchengebühren erfolgte ohne Widerspruch.

WEITERE ANGABEN PCT/ISA/ 210

Die internationale Recherchenbehörde hat festgestellt, dass diese internationale Anmeldung mehrere (Gruppen von) Erfindungen enthält, nämlich:

1. Ansprüche: 1-10 (ganz) und 31-36, 50, 51, 53 (zum Teil)

   Verwendung von Annexin A3 als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

---

2. Ansprüche: 11, 12, 38, 39 (ganz) und 28-30, 36, 46-49, 51, 53 (zum Teil)

   Verwendung von Enoyl-Coenzym A-Hydratase als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

---

3. Ansprüche: 13-14, 28-30, 37, 46-49, 51 (alle zum Teil)

   Verwendung von Protein-Disulfid-Isomerase (PDI) als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

---

4. Ansprüche: 13, 14, 27-30, 36, 37, 46-51, 53 (alle zum Teil)

   Verwendung von Ubiquitin-Isopeptidase T als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

---

5. Ansprüche: 15, 16, 40 (ganz) und 27, 31-36, 41, 46-49, 51, 53 (zum Teil)

   Verwendung von Serum-Amyloid P-Komponente (SAP) als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

---

6. Ansprüche: 17, 18, 41 (ganz) und 31-36, 41, 46-49, 51, 53 (zum Teil)

   Verwendung von nukleäres Chloridionenkanal-Protein als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

---

7. Ansprüche: 19, 20, 42 (ganz) und 46-49, 51, 53 (zum Teil)

   Verwendung von HES1 als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

WEITERE ANGABEN PCT/ISA/ 210

8. Ansprüche: 21, 22, 43 (ganz) und 46-49, 51, 53 (zum Teil)

Verwendung von Proteasomen alpha 2-Untereinheit als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

---

9. Ansprüche: 23, 24, 44 (ganz) und 46-49, 51, 53 (zum Teil)

Verwendung von Adenin-Phosphoribosyltransferase als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

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10. Ansprüche: 25, 26, 45 (ganz) und 46-49, 51, 53 (zum Teil)

Verwendung von anorganische Pyrophosphatase als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

---

11. Ansprüche: 28-30, 50, 51 (alle zum Teil)

Verwendung von Hitzeschockprotein 27 (HSP27) als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

---

12. Ansprüche: 28-30, 50, 51, (alle zum Teil)

Verwendung von Hitzeschockprotein 90 (HSP90) als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

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13. Ansprüche: 28-30, 51 (alle zum Teil)

Verwendung von Nucleophosmin als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

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14. Ansprüche: 31-35, 50, 51 (alle zum Teil)

Verwendung von Fettsäurebindendes Protein 3 (FABP-3) als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

---

15. Ansprüche: 31-35, 50, 51 (alle zum Teil)

Verwendung von Galektin als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

WEITERE ANGABEN PCT/ISA/ 210

16. Ansprüche: 31-35, 50, 51 (alle zum Teil)

Verwendung von Mikrosemenoprotein beta als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

17. Ansprüche: 31-35, 51 (alle zum Teil)

Verwendung von 14-3-3 Protein beta als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

18. Ansprüche: 31-35, 51 (alle zum Teil)

Verwendung von 14-3-3 Protein zeta als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

19. Ansprüche: 31-35, 51, 53 (alle zum Teil)

Verwendung von 14-3-3 Protein tau als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

20. Ansprüche: 31, 33-35, 51 (alle zum Teil)

Verwendung von epidermales Fettsäure bindendes Protein (E-FABP) als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

21. Ansprüche: 31-35, 50, 51 (alle zum Teil)

Verwendung von Transgelin als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

22. Ansprüche: 31-35, 51 (alle zum Teil)

Verwendung von Triosephosphat-Isomerase als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

23. Ansprüche: 31-35, 51 (alle zum Teil)

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Verwendung von Aldolase A als diagnostischer Marker für Prostatakrebs sowie als Target für die Behandlung von Prostatakrebs.

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